REMARKS/ARGUMENTS

The December 18, 2003 Office Action has rejected all claims under 35 U.S.C. § 112, 35 U.S.C. § 102 and 35 U.S.C. § 103. In light of the amendments above, the enclosed Exhibits and the arguments below, Applicants respectfully request reconsideration.

§ 112 Rejections

Claims 1 – 5 are rejected under 35 U.S.C. § 112 on the ground that the specification "while being enabling for methods of reducing the risk of onset of Type 1 diabetes in patients with autoantibodies toward glutamic acid decarboxylase or insulin, does not reasonably provide enablement for methods of eliminating the onset or absolutely preventing such diabetes in any human patients." Applicants do not agree that the specification has not enabled eliminating the onset of Type 1 diabetes, but have acceded to the Examiner's wishes by amending claim 1 (with the Examiner's suggested language) to a method of reducing the risk of Type 1 diabetes in a predisposed human patient by up to 90 percent and added new claims 6 - 15 with the Examiner's alternative suggested language to a method of reducing the risk of onset of Type 1 diabetes in patients with autoantibodies towards glutamic acid decarboxylase.

Claims 1 – 5 are rejected as being indefinite. Applicants have clarified claim 1 language.

§ 102 Rejections

Claims 1 – 5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mathieu, et al. Applicants note that Mathieu does not teach oral administration to the patient and does not teach reducing the risk by up to 90 percent, as the claims now require.

§ 103 Rejections

Claims 1 – 5 are rejected under 35 U.S.C. § 103 as being unpatentable over Mathieu, et al. in view of EURODIAB, Mauricio, et al., DeWille, et al. and Facts and Comparison 1999. Applicants strenuously assert that one of skill in the art would not combine the Examiner's cited art to produce the currently claimed invention.

The Examiner has cited EURODIAB and Muricio as collectively providing the understanding that "vitamin D and analogues thereof . . . improve the symptoms of autoimmune diseases and diabetes. . ." Applicants first note that these references do not teach oral administration, which Applicant believes is critical.

Applicants first address the Examiner's assertion that "the term vitamin D generic that describes all steroids that exhibit qualitatively the biological activity of colicalciferol . . . according to 1α hydroxyvitamin D is encompassed by such definition of vitamin D . . . ." Applicants do not wish to belabor the use of the phrase "ordinary" to describe vitamin D. Applicants wish to claim that 1α hydroxyvitamin D is what is claimed and that compounds that are not part of this group would not have been expected to act similarly.

Applicants point out to Examiner that the authors in EURODIAB do not describe 1α hydroxyvitamin D as reducing the risk of developing Type I Diabetes. The present invention does not claim and, in fact, teaches away from the use of the vitamin D compounds described in EURODIAB to prevent diabetes. For example, Applicants note that NOD mice used in the examples of the specification have sufficient amounts of vitamin D in their diet. These animals developed diabetes quite clearly (as disclosed in the specification and previous work in the field) so vitamin D itself cannot prevent diabetes.

The Office Action makes the statement that "all vitamin D within its generic meaning are expected to provide similar clinical benefit." Applicants note for the Examiner that this is not correct and have enclosed, as a Supplemental Information Disclosure Statement, several article demonstrating the difference between the activities of a particular analog of vitamin D. For example, Slatopolsky, et al. demonstrate that renal osteodystrophy was successfully treated by 1,25-dihydroxyvitamin D_3 as was another analog, 22 oxa 1,25 dihydroxyvitamin D_3. Vitamin D itself, which would have been present in these patients' diet, was not effective.

As for the Examiner's next citation, Applicants read Mauricio, et al. as discussing the role of 1,25 D_3 in diabetes and numerous other autoimmune diseases. A reading of Mauricio indicates that use of 1,25 D_3 may or may not be successful in diabetes treatment. It is certainly not possible to read Mauricio as teaching that 1,25 D_3 would necessarily be a successful diabetes treatment. Note the first paragraph in the right hand column on page 63, "However, this is still a matter of controversy since recent data on the effects of 1,25 D_3 on influence secretion *in vitro* showed no effect on glucose-stimulated insulin secretion on rat islet . . . or even an inhibition by 1,25 D_3 on rat islet cultures and RIN cells. Although in light of some of these studies the application of 1,25 D_3 as an enhancer of insulin secretion has been proposed in the field of diabetes mellitus, further research is warranted." (emphasis added).

Applicants further point out that claim 1 recites oral administration, "such that the risk onset of diabetes or diabetes symptoms is reduced by up to 90%." As discussed above, the specification teaches more than improving or treating symptoms of diabetes in general, but teaches prevention or reduction of the onset of diabetes at a particular efficacy. Mathieu, in

combination with EURODIAB and Muricio, clearly does not provide the understanding that oral administration of 1α-hydroxy vitamin D compound achieves this goal.

Examiner next cites DeWille and Facts and Comparisons to show that "all vitamin D . . . can be prepared and used orally." However, as applicants point out above, DeWille does not teach oral administration to diabetes patients. Facts and Comparisons also does not list diabetes or any autoimmune disease as an indication for which any form of vitamin D should be administered. Applicants are not disputing that DeWille and Facts and Comparisons teach oral administration of vitamin D. However, Applicants point out that DeWille and Facts and Comparisons, in combination Mathieu, EURODIAB and Muricio, do not teach oral administration of 1α-hydroxy vitamin D as a uniquely successful mode of administration for reducing the risk of diabetes by up to 90%.

Therefore, Applicants assert that one could not combine the Examiner's cited references to teach the success of the Applicants' cited compounds and mode of administration in treating Type I diabetes.

New Matter Rejection

Claims 1 – 5 are rejected as containing "subject matter which was not described in the specification . . . ." The Examiner has suggested that a phrase in claim 1 is not fully supported by the specification. Although Applicants do not agree, Applicants have removed the expression "β cell antigens" from both claim 1 and new independent claim 6. Applicants trust that this rejection is now moot.

Applicants believe that the claims are in condition for allowance and respectfully request allowance. Applicants have enclosed a Petition and Fee for two months extension of

time and Request for Continued Examination (RCE). No other fees are believed necessary. However, if a fee is necessary please charge Deposit Account 17-0055.

Respectfully submitted,

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